

09/708,974

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L4 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:793447 CAPLUS
 TITLE: Modulators of hedgehog signaling pathway for treatment of T-cell-mediated diseases
 INVENTOR(S): Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman, Margaret Jane; Champion, Brian Robert
 PATENT ASSIGNEE(S): Loralantis Limited, UK
 SOURCE: PCT Int. Appl., 154 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002080952	A2	20021017	WO 2002-GB1666	20020409

V: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MW, MX, MY, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

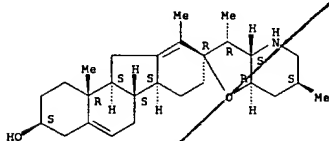
PRIORITY APPLN. INFO.: GB 2001-8872 A 20010409
 GB 2001-8873 A 20010409

AB Use of a modulator of a Hedgehog signaling pathway, or a modulator of a pathway which is a target of the Hedgehog signaling pathway in the prep. of a medicament for treatment of a disease or disorder assocd. with a T-cell mediated disease or disorder.

IT 4449-51-8, Cyclopamine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (modulators of hedgehog signaling pathway for treatment of T-cell-mediated diseases)

RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:777728 CAPLUS
 DOCUMENT NUMBER: 137:257646
 TITLE: Use of cyclopamine in the treatment of basal cell carcinoma and other tumors
 INVENTOR(S): Avci, Oktay
 PATENT ASSIGNEE(S): Tas, Sinan, Turk.
 SOURCE: PCT Int. Appl., 19 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002078703	A1	20021010	WO 2001-TR27	20010702

V: AT, AU, BR, CA, CN, DE, DK, ES, FI, GB, IN, JP, MX, NO, PT, RU, SE, TR, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

WO 2002078704 A1 20021010 WO 2002-TR17 20020419

V: AT, AU, BR, CA, CN, DE, DK, ES, FI, GB, IN, JP, MX, NO, PT, RU, SE, TR, US

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

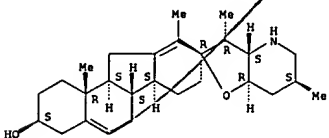
PRIORITY APPLN. INFO.: WO 2001-TR27 A 20010702

AB The invention concerns the use of cyclopamine in vivo on basal cell carcinomas to achieve therapeutic effect by causing differentiation of the tumor cells and, at the same time, highly efficient apoptotic death and removal of these tumor cells while preserving the normal tissue cells, including the undifferentiated cells of the normal epidermal basal layer and hair follicles. Causation of apoptosis by cyclopamine is by a non-genotoxic mechanism. These effects make the use of cyclopamine highly desirable in the treatment of basal cell carcinomas and other tumors that use the hedgehog/smoothed signal transduction pathway for proliferation and prevention of apoptosis.

IT 4449-51-8, Cyclopamine
 RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Use of cyclopamine in the treatment of basal cell carcinoma and other tumors)

RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



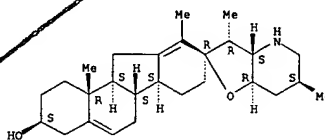
L4 ANSWER 1 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

L4 ANSWER 2 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

IT 4449-51-8D, Cyclopamine, derivs.
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Use of cyclopamine in the treatment of basal cell carcinoma and other tumors)

RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:293477 CAPLUS
 DOCUMENT NUMBER: 136:304056
 TITLE: Hedgehog antagonists, methods and uses related thereto
 INVENTOR(S): Dudek, Henryk; Picicelli, Carmen; Karavanov, Irina
 PATENT ASSIGNEE(S): Curis, Inc., USA
 SOURCE: PCT Int. Appl., 224 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030462	A2	20020418	WO 2001-US32100	20011015
V: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002165221	A1	20021107	US 2001-977096	20011012
AU 2001096844	A5	20020422	AU 2001-96844	20011015
PRIORITY APPLN. INFO.: US 2000-240564P P 20001013 US 2000-240536P P 20001013 WO 2001-US32100 W 20011016				

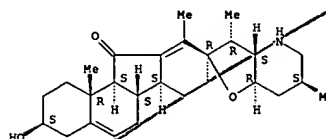
AB The present application is directed to compns. and methods for inhibiting angiogenesis and treating or preventing unwanted cell proliferation, including tumors, by inhibiting the hedgehog pathway, e.g., with an antagonist of the hedgehog pathway such as those disclosed herein. In one embodiment, the subject methods may be used to inhibit unwanted cell proliferation by detg. whether cells overexpress a gli gene, and contacting cells that overexpress gli gene with an effective amt. of a hedgehog antagonist. In preferred embodiments, the unwanted cell proliferation is cancer or benign neoplastic hyperplasia. Another aspect of the present invention involves measuring the levels of gli gene expression in order detn. the likelihood that a cancer will develop or to detn. a cancer treatment protocol. Another embodiment of the invention involves methods for using hedgehog antagonists to stimulate surfactant prodn. or lamellated body formation in lung cells, esp. the lung cells of premature infants. In other preferred embodiments, hedgehog antagonists are selected from small mols., hedgehog antibodies, antisense nucleic acids and ribozymes.

IT 469-59-0, Jervine 4449-51-8, Cyclopamine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (hedgehog pathway antagonists for inhibition of unwanted cell proliferation in cells overexpressing gli gene or to stimulate surfactant prodn. in lung for treatment of premature infants)

RN 469-59-0 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one, 2,3,3',4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

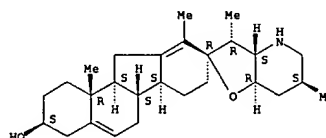
L4 ANSWER 3 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3',4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:507523 CAPLUS
 DOCUMENT NUMBER: 135:87198
 TITLE: Use of steroidal alkaloids to reverse multidrug resistance
 INVENTOR(S): Lisacovitch, Mordechai; Lavie, Yaakov
 PATENT ASSIGNEE(S): Yeda Research and Development Co. Ltd., Israel
 SOURCE: PCT Int. Appl., 31 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

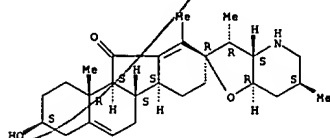
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001049279	A2	20010712	WO 2000-11866	20001228
V: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PK, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.: IL 1999-133809 A 19991230				

AB The invention provides steroidal alkaloids for inhibiting or reversing multidrug resistance in cancer or in bacterial, fungal or parasitic infections. The steroidal alkaloid may be administered to the patient alone or in combination with an anticancer, antibacterial, antifungal or antiparasitic agent. Examples of steroidal alkaloids include members of the solanidane or spirosolane families (e.g. tomatidine), and C-nor-D-homo steroids, e.g. of the jervane or veratramine families.

IT 469-59-0, Jervine 4449-51-8, Cyclopamine
 14788-78-4 19773-24-1, Peimine 24508-94-9
 Tetrahydrojervine 212968-58-6, Verapaputine 347842-64-2
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (steroidal alkaloids for reversal of multidrug resistance)

RN 469-59-0 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one, 2,3,3',4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

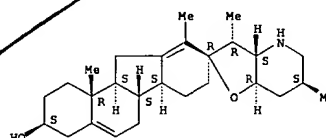
Absolute stereochemistry.



L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

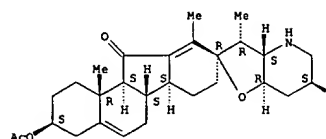
RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3',4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 14788-78-4 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(2H)-one, 3-(acetyloxy)-1,3,3',4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

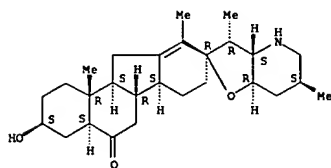
Absolute stereochemistry.



RN 19773-24-1 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-5(6H)-one, 1,2,3,3',4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

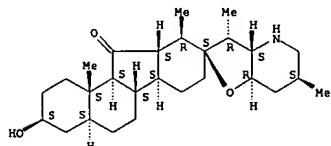
Absolute stereochemistry.

L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)



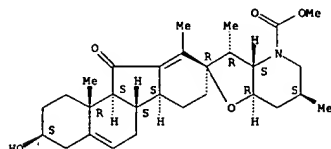
RN 24508-94-9 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(2H)-one, 1,2,3,3'a,4,4'a,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,4aS,6'S,6aS,6bS,7'aR,10R,10aS,11aS,11bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 212968-58-6 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridine]-4'-(3'aH)-carboxylic acid, 1,2,3,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-11-oxo-, methyl ester, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS

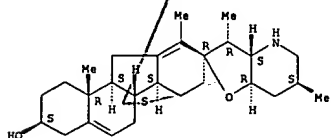
ACCESSION NUMBER: 2001:447066 CAPLUS
 DOCUMENT NUMBER: 136:210143
 TITLE: Inhibitory effect of steroidal alkaloids on drug transport and multidrug resistance in human cancer cells
 AUTHOR(S): Lavie, Yaakov; Harel-Orbital, Tovi; Gaffield, William; Liscovitch, Mordechai
 CORPORATE SOURCE: Department of Biological Regulation, Weizmann Institute of Science, Rehovot, 76100, Israel
 SOURCE: Anticancer Research (2001), 21(2A), 1189-1194
 CODEN: ANTRD4; ISSN: 0250-7005
 PUBLISHER: International Institute of Anticancer Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Intrinsic or acquired resistance of tumor cells to multiple cytotoxic drugs (multidrug resistance, MDR) is a major cause of failure of cancer chemotherapy. MDR is often caused by elevated expression of drug transporters such as P-glycoprotein (P-gp) or multidrug resistance protein (MRP). A no. of compds., termed chemosensitizers, have little or no cytotoxic action of their own, but inhibit (P-gp) or MRP-mediated drug export and are capable of sensitizing MDR cells to the cytotoxic effects of chemotherapeutic drugs. Here the authors examd. the ability of steroidal alkaloids of plant origin, namely the Veratrum sp. alkaloid cyclopamine and the Lycopersicon sp. alkaloid tomatidine, to act as potent and effective chemosensitizers in multidrug resistant tumor cells. Drug uptake was detd. by measuring accumulation of tetramethylrosamine in multidrug resistant NCI AdR human adenocarcinoma cells. Resistance to adriamycin and vinblastine was detd. by utilizing the MTT cell survival assay. Cyclopamine and tomatidine elevate tetramethylrosamine uptake by NCI AdR cells and sensitize the cells to the cytotoxic action of adriamycin and vinblastine. In both cases these agents are comparable in patency and efficacy to verapamil, a reversal agent commonly used in MDR research. It is concluded that steroidal alkaloids of plant origin act as inhibitors of P-gp-mediated drug transport and multidrug resistance and therefore may serve as chemosensitizers in combination chemotherapy with conventional cytotoxic drugs for treating multidrug resistant cancer.

IT 4449-51-8, Cyclopamine
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inhibitory effect of steroidal alkaloids on drug transport and multidrug resistance in human cancer cells)

RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4'a,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

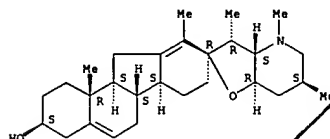
Absolute stereochemistry.



L4 ANSWER 4 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 347842-64-2 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4'a,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-pentamethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 5 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:434884 CAPLUS

DOCUMENT NUMBER: 135:41031

TITLE: Methods using hedgehog protein or hedgehog protein-encoding nucleic acid to stimulate insulin production by pancreatic .beta.-cells

INVENTOR(S): Habener, Joel F.; Thomas, Melissa K.

PATENT ASSIGNEE(S): The General Hospital Corporation, USA

SOURCE: PCT Int. Appl., 63 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041786	A1	20010614	WO 2000-US33575	20001208
V: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-170282P P 19991210

AB The invention features a method of treating deficiency of insulin in a patient, comprising administering to a patient in need thereof hedgehog protein or nucleic acid in an amt. effective to raise the level of insulin in the patient. A method is also disclosed for suppressing insulin secretion using hedgehog protein inhibitor, e.g. cyclopamine.

IT 4449-51-8, Cyclopamine 4449-51-8D, Cyclopamine, derivs.

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

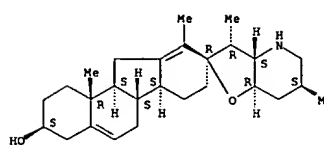
(hedgehog protein or hedgehog protein-encoding nucleic acid to stimulate insulin prodn. by pancreatic .beta.-cells)

RN 4449-51-8 CAPLUS

CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

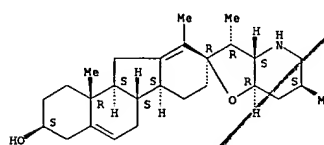
L4 ANSWER 6 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 4449-51-8 CAPLUS

CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4

THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:283977 CAPLUS

DOCUMENT NUMBER: 134:295995

TITLE: Synthesis, compositions and uses of steroidal alkaloids as regulators of the hedgehog pathway

INVENTOR(S): Beachy, Philip A.

PATENT ASSIGNEE(S): Johns Hopkins University School of Medicine, USA

SOURCE: PCT Int. Appl., 164 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027135	A2	20010419	WO 2000-US28479	20001013
WO 2001027135	A3	20020510		
V: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

EP 1235851 A2 20020904 EP 2000-973544 20001013

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL

PRIORITY APPLN. INFO.: US 1999-159215P P 19991013

US/2000-229273P P 20000830

WO 2000-US28479 W 20001013

OTHER SOURCE(S): MARPAT 134:295995

AB The present invention makes available, inter alia, methods and reagents for modulating smoothened-dependent pathway activation. In certain embodiments, the subject methods can be used to counteract the phenotypic effects of unwanted activation of a hedgehog pathway, such as resulting from hedgehog gain-of-function, ptc loss-of-function or smoothened gain-of-function mutations. Synthesis of cyclopamine, jervine and cyclopamine derivs. is presented.

IT 334616-90-6P 334616-24-9P 334616-28-3P

334616-33-0P 334616-35-2P 334616-36-3P

334616-43-2P 334616-45-4P 334616-53-4P

334616-56-7P 334616-63-6P 334616-69-2P

334616-70-5P 334616-75-0P 334616-76-1P

334658-24-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(synthesis, compns. and uses of steroidal alkaloids as regulators of the hedgehog pathway)

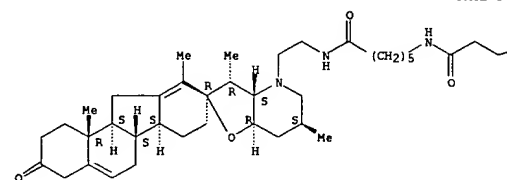
RN 334616-90-6 CAPLUS

CN Benzenepropanamide, N-[6-[[2-[(3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-3-oxospiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]amino]-6-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

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PAGE 1-B

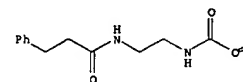
Ph

RN 334616-24-9 CAPLUS

CN Carbanic acid, [2-[(1-oxo-3-phenylpropyl)amino]ethyl]-, (3S,3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-yl ester (9CI) (CA INDEX NAME)

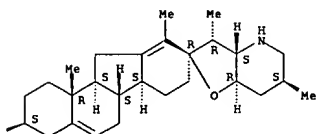
Absolute stereochemistry.

PAGE 1-A



L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

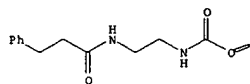
PAGE 1-B



RN 334616-28-3 CAPLUS
 CN Carbamic acid, [2-[(1-oxo-3-phenylpropyl)amino]ethyl]-, (3S,3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-11-oxospiro[9H-benzo[a]fluorene-9,2'(3'H)-furo[3,2-b]pyridin]-3-yl ester (9CI) (CA INDEX NAME)

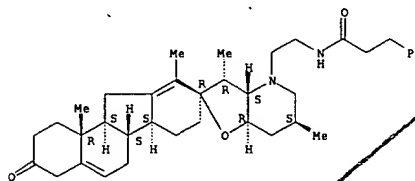
Absolute stereochemistry.

PAGE 1-A



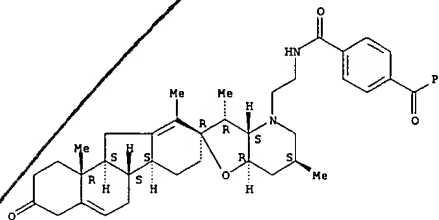
L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)
 b]pyridin]-4'-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 334616-35-2 CAPLUS
 CN Benzamide, 4-benzoyl-N-[2-[(3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-3-oxospiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]- (9CI) (CA INDEX NAME)

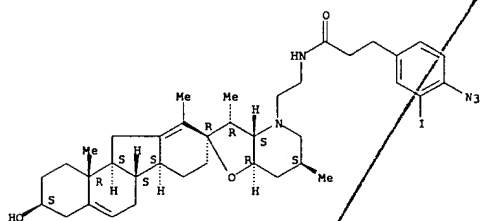
Absolute stereochemistry.



RN 334616-36-3 CAPLUS
 CN Benzenepropanamide, 4-azido-3-iodo-N-[2-[(3S,3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]- (9CI) (CA INDEX NAME)

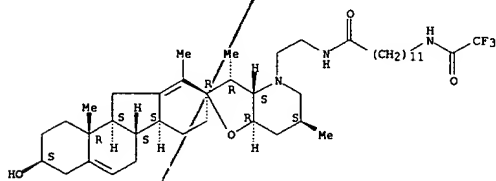
Absolute stereochemistry.

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 334616-43-2 CAPLUS
 CN Dodecanamide, N-[2-[(3S,3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]-12-[(trifluoroacetyl)amino]- (9CI) (CA INDEX NAME)

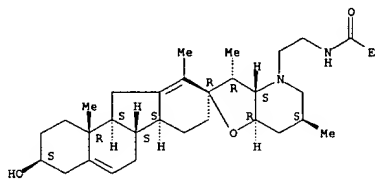
Absolute stereochemistry.



RN 334616-45-4 CAPLUS
 CN Propanamide, N-[2-[(3S,3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

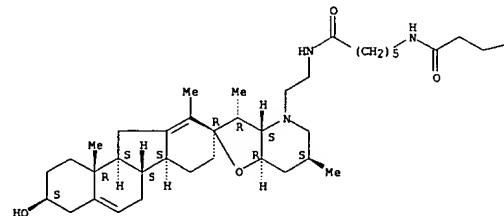
L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)



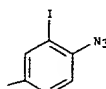
RN 334616-53-4 CAPLUS
 CN Benzenepropanamide, 4-azido-3-iodo-N-[6-[(3S,3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]amino]-6-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

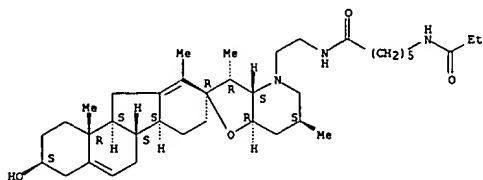


PAGE 1-B



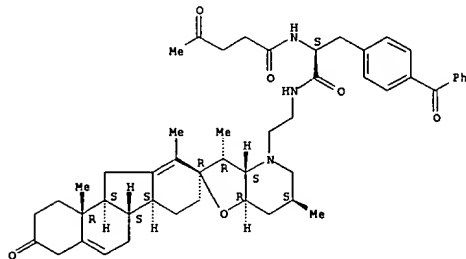
L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 334616-56-7 CAPLUS
CN Hexanamide, N-[2-[(3S,3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]-6-[(1-oxopropyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 334616-63-6 CAPLUS
CN Benzenepropanamide, 4-benzoyl-.alpha.-[(1,4-dioxopentyl)amino]-N-[2-[(3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-3-oxospiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)

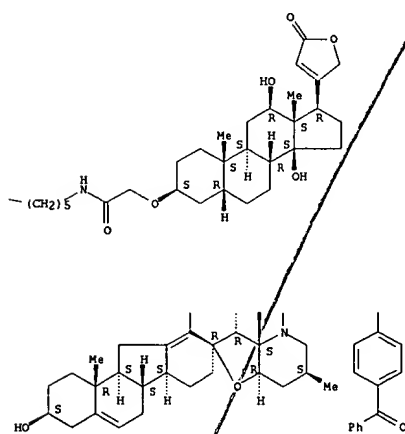
Absolute stereochemistry.



RN 334616-69-2 CAPLUS
CN Card-20(22)-enolide, 3-[2-[[6-[[5-[(4-benzoylbenzoyl)amino]-6-[[2-[(2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-1,2,3,3',3'a,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

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PAGE 2-A

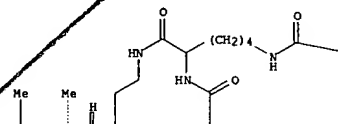
RN 334616-70-5 CAPLUS
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[6-[[5-[(4-benzoylbenzoyl)amino]-6-[[2-[(2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]amino]-6-oxohexyl]hexahydro-2-oxo-, (3aS,4S,6aR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)
hydroxy-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]amino]-6-oxohexyl]amino]-2-oxoethyl]amino]-2-oxohexyl]hexahydro-2-oxo-, (3aS,4S,6aR)- (9CI) (CA INDEX NAME)

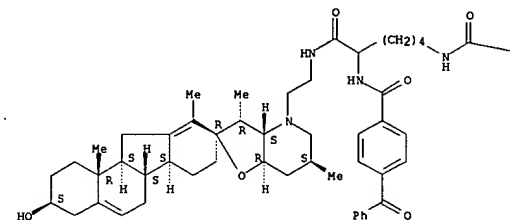
Absolute stereochemistry.

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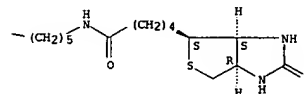


L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

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PAGE 1-B

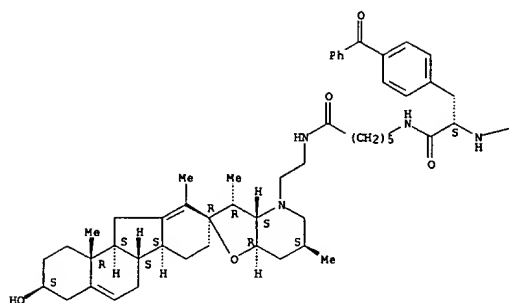


RN 334616-75-0 CAPLUS
CN 1H-Thieno[3,4-d]imidazole-4-pentanamide, N-[6-[[5-[(4-benzoylbenzoyl)amino]-6-[[2-[(2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-1,2,3,3',3'a,4,5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'(4'H)-furo[3,2-b]pyridin]-4'-yl]ethyl]amino]-6-oxohexyl]amino]-2-oxoethyl]amino]-2-oxohexyl]hexahydro-2-oxo-, (3aS,4S,6aR)- (9CI) (CA INDEX NAME)

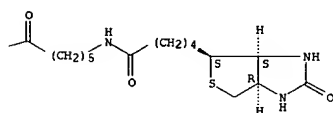
Absolute stereochemistry.

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

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PAGE 1-B

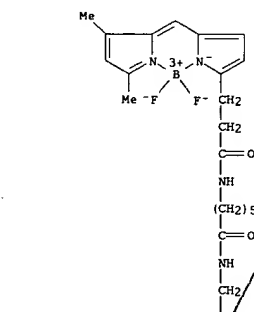


RN 334616-76-1 CAPLUS
 CN Benzenepropanamide, 4-azido-3-(iodo-125I)-N-[6-[[2-
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 3',6',10,11b-tetramethylspiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-
 b]pyridin]-4'-yl]ethyl]amino]-6-oxohexyl]- (9CI) (CA INDEX NAME)

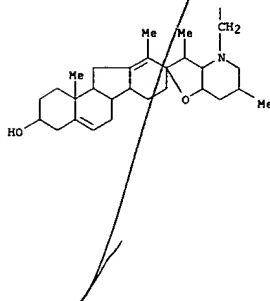
Absolute stereochemistry.

L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A

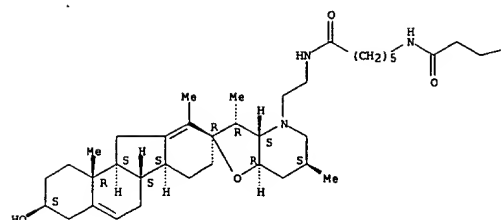


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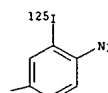


L4 ANSWER 7 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

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RN 334658-24-1 CAPLUS
 CN Beron, [5-[(3,5-dimethyl-2H-pyrrol-2-ylidene-kappa.N)methyl]-N-[6-[[2-
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 b]pyridin]-4'-yl]ethyl]amino]-6-oxohexyl]-1H-pyrrole-2-propanamidato-
 -kappa.N]difluoro-, (7-4)- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:880985 CAPLUS
 DOCUMENT NUMBER: 134:37058
 TITLE: Therapeutic use of an inhibitor of a hedgehog or a
 hedgehog-related signaling pathway
 INVENTOR(S): Lamb, Jonathan Robert; Hoyne, Gerard Francis; Dallman,
 Margaret Jane
 PATENT ASSIGNEE(S): Lorantis Limited, UK
 SOURCE: PCT Int. Appl., 78 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000074706	A1	20001214	WO 2000-GB2191	20000605
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1181040	A1	20020306	EP 2000-935413	20000605
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PRIORITY APPLN. INFO.:				
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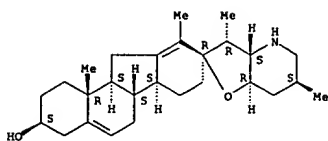
AB Use of an inhibitor of a Hedgehog signaling pathway, or an inhibitor of a pathway which is a target of the Hedgehog signaling pathway in the prep. of a medicament for treatment of epithelial cell hyperplasia, fibrosis of tissue, inflammation, cancer or an immune disorder. Also a transgenic animal or cell line capable of expressing a component or an inhibitor of a hedgehog signaling pathway or a target pathway of the hedgehog signaling pathway.

IT 4449-51-8, Cyclopamine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Therapeutic use of inhibitor of hedgehog protein or hedgehog-related signaling pathway and transgenic animal or cell line expressing component or inhibitor of these pathways)

RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 8 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2002 ACS

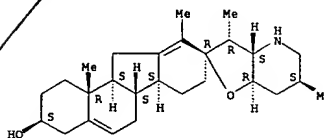
ACCESSION NUMBER: 2000:637045 CAPLUS
DOCUMENT NUMBER: 133:344307
TITLE: Effects of oncogenic mutations in Smoothened and Patched can be reversed by cyclopamine
AUTHOR(S): Taipale, Jussi; Chen, James K.; Cooper, Michael K.; Wang, Baolin; Mann, Randall K.; Milenkovic, Ljiljana; Scotts, Matthew P.; Beachy, Philip A.
CORPORATE SOURCE: Department of Molecular Biology and Genetics, The Johns Hopkins University School of Medicine, Baltimore, MD, 21205, USA
SOURCE: Nature (London) (2000), 406(6799), 1005-1009
CODEN: NATUAS; ISSN: 0028-0836
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Basal cell carcinoma, medulloblastoma, rhabdomyosarcoma and other human tumors are assocd. with mutations that activate the proto-oncogene Smoothened (SMO) or that inactivate the tumor suppressor Patched (PTCH). Smoothened and Patched mediate the cellular response to the Hedgehog (Hh) secreted protein signal, and oncogenic mutations affecting these proteins cause excess activity of the Hh response pathway. Here we show that the plant-derived teratogen cyclopamine, which inhibits the Hh response, is a potential 'mechanism-based' therapeutic agent for treatment of these tumors. We show that cyclopamine or synthetic derivs. with improved potency block activation of the Hh response pathway and abnormal cell growth assocd. with both types of oncogenic mutation. Our results also indicate that cyclopamine may act by influencing the balance between active and inactive forms of Smoothened.

IT 4449-51-8, Cyclopamine 306387-90-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of oncogenic mutations in Smoothened and Patched can be reversed by cyclopamine)

RN 4449-51-8 CAPLUS
CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

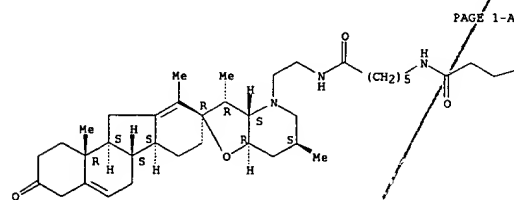


RN 306387-90-6 CAPLUS
CN Benzenepropanamide, N-[6-[[2-[(3'R,3'aS,6'S,6aS,6bS,7'aR,2'R,11aS,11bR)-

L4 ANSWER 9 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-3-oxospiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-4'-yl]ethylamino]-6-oxohexyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-A

PAGE 1-B

Ph

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:993313 CAPLUS
DOCUMENT NUMBER: 133:99549
TITLE: Regulation of the hedgehog pathway and smoothened gain-of-function by gene patched agonists
INVENTOR(S): Dudek, Henryk; Ji, Benxiu
PATENT ASSIGNEE(S): Ontogeny, Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000041545	A2	20000720	WO 2000-US873	20000113
WO 2000041545	A3	20000928		
V: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6291516	B1	20010918	US 1999-417564	19991014
EP 1143961	A2	20010107	EP 2000-906910	20000113
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 2001034337	A1	20011025	US 2001-867311	20010529
PRIORITY APPLN. INFO.: US 1999-115642P P 19990113				
US 1999-119594P P 19990210				
US 1999-142124P P 19990702				
US 1999-417564 A 19991014				
WO 2000-US873 W 20000113				

OTHER SOURCE(S): MARPAT 133:99549

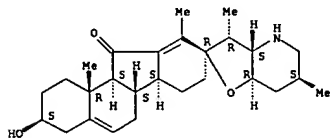
AB The present invention makes available methods and reagents for inhibiting aberrant growth states resulting from hedgehog gain-of-function, patched (ptc) loss-of-function or smoothened gain-of-function comprising contacting a cell with a compd., such as a polypeptide or small mol. in an amt. sufficient to control the aberrant growth state, e.g., to agonize a normal ptc pathway or antagonize smoothened or hedgehog activity. The present invention further makes available methods and reagents for ameliorating the consequences of hedgehog loss-of-function, ptc gain-of-function, or smoothened loss-of-function comprising contacting a cell with a compd., such as a polypeptide or small mol., in an amt. sufficient for amelioration. In certain embodiments, the subject compds., e.g., a cAMP analog, adenylate cyclase agonist, or cAMP phosphodiesterase inhibitor, regulate cAMP levels, which in turn modulates activity of the hedgehog pathway. Thus, compds. such as jervine, cyclopamine, and forskolin analogs are also effective in inhibition of medulloblastoma.

IT 469-59-0, Jervine 4449-51-8, Cyclopamine
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regulation of the hedgehog pathway and smoothened gain-of-function by gene patched agonists)

RN 469-59-0 CAPLUS
CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one,

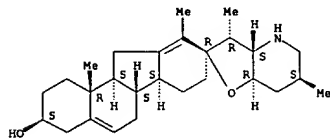
L4 ANSWER 10 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)
 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-
 3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol,
 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-octadecahydro-
 3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:38438 CAPLUS

DOCUMENT NUMBER: 132:202865

TITLE:

Effects of Veratrum nigrum alkaloids on central catecholaminergic neurons of renal hypertensive rats

Li, Huar Gao, Guang-You Li, Shu-Yuan

Department of Pharmacology, Dalian Medical University,

Dalian, 116027, Peop. Rep. China

SOURCE: Acta Pharmacologica Sinica (2000), 21(1), 23-28

CODEN: APSGGS

PUBLISHER: Science Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Aim: To study the central hypotensive mechanism of Veratrum nigrum L var ussuriense Nakai alkaloids (VnA) in renal hypertensive rats (RHR). Methods: The quant. method of immunocytochem. (ICC) was used to observe and detect the effect of VnA (30 .mu.g .cntdot. kg-1, iv) on activity of central catecholaminergic (CA) neurons of C1, C2, A1, and A5 areas in RHR. Results: VnA increased the immunoreactivity (IR) of tyrosine 3-monooxygenase (TH)-immunopos. (IP) neurons of C1, C2, and A5 areas in RHR expst. group compared with RHR control group [pos. units: (1.9.+-0.4), (1.18.+-0.23), (1.2.+-0.4) vs (0.15.+-0.22), (0.31.+-0.16), (0.69.+-0.20), resp.]; IR of TH-IP neurons of C1 and C2 areas in RHR control group was decreased compared with sham-operated group [pos. units: (0.15.+-0.22), (0.31.+-0.16) vs (1.45.+-0.29), (1.36.+-0.25), resp.]. Conclusion: VnA increased the activity of central CA neurons in RHR to exert its hypotensive effect.

IT 469-59-0, Jervine

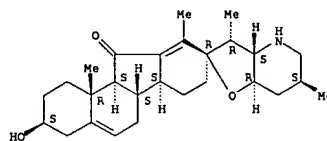
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Veratrum nigrum alkaloids effect on central catecholaminergic neurons in renal hypertension)

RN 469-59-0 CAPLUS

CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one,
 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-
 3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:672583 CAPLUS

DOCUMENT NUMBER: 131:267077

TITLE: Use of steroidal alkaloid derivatives as inhibitors of hedgehog signaling pathways

Beachy, Philip A.; Cooper, Michael K.; Porter, Jeffrey A.

Patent Assignee(s): Johns Hopkins University School of Medicine, USA

SOURCE: PCT Int. Appl., 136 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9952534	A1	19991021	WO 1999-057811	19990409
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
US 2002006931	A1	20020117	US 1998-90622	19980604
US 6432970	B2	20020813		
CA 2326654	AA	19991021	CA 1999-2326654	19990409
AU 9934860	A1	19991101	AU 1999-34860	19990409
EP 1067939	A1	20010117	EP 1999-916563	19990409
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002511415	T2	20020416	JP 2000-543144	19990409
PRIORITY APPL. INFO.:			US 1998-81186P	P 19980409
			US 1998-81263P	P 19980409
			US 1998-90622	A 19980604
			WO 1999-057811	W 19990409

OTHER SOURCE(S): MARPAT 131:267077

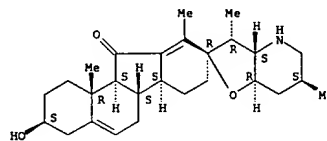
AB The present invention makes available assays and reagents inhibiting paracrine and/or autocrine signals produced by a hedgehog protein or aberrant activation of a hedgehog signal transduction pathway, e.g., which involve the use of a steroidal alkaloid or other small mol.

IT 469-59-0, Jervine 4449-51-8, Cyclopamine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (Use of steroidal alkaloid derivs. as inhibitors of hedgehog signaling pathways in relation to effect on cholesterol biosynthesis)

RN 469-59-0 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one,
 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-
 3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.

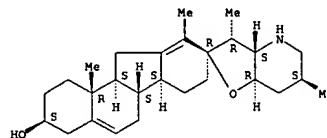
L4 ANSWER 12 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 4449-51-8 CAPLUS

CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one,
 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-
 3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-
 (9CI) (CA INDEX NAME)

Absolute stereochemistry.



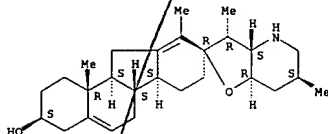
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 16 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:639750 CAPLUS
 DOCUMENT NUMBER: 131:331613
 TITLE: A looking glass perspective: thalidomide and cyclopamine
 AUTHOR(S): Gaffield, William; Incardona, John P.; Kapur, Raj P.; Roelink, Henk
 CORPORATE SOURCE: Western Regional Research Center, ARS, USDA, Albany, CA, 94710, USA
 SOURCE: Cellular and Molecular Biology (Paris) (1999), 45(5), 579-588
 CODEN: CMOBEF; ISSN: 0145-5680
 PUBLISHER: C.M.B. Association
 DOCUMENT TYPE: Journal; General Review
 LANGUAGE: English

AB A review with many refs. Numerous naturally-occurring and synthetic compds. that were discovered initially because of their toxic properties, were later shown to possess biol. activities beneficial to humans that enabled them to serve as templates for the development of useful medicinal agents. A prominent example is thalidomide, a synthetic drug that gained notoriety originally due to its catastrophic teratogenicity in humans. The discovery of thalidomide's efficacy in treating several diseases has resulted in the recrudescence of the drug to society's usage. A current example of this phenomenon is the plant teratogen cyclopamine (11-deoxojervine), whose deleterious terata-inducing effects were restricted to grazing animals, but whose recently discovered inhibition of Sonic hedgehog signal transduction has provided both the potential to increase our understanding of organogenesis and to serve as a lead compd. in drug development.

IT 4449-51-8, Cyclopamine
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (thalidomide and cyclopamine)
 RN 4449-51-8 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

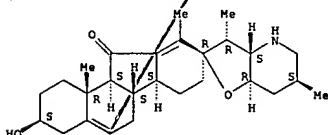
L4 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:436553 CAPLUS
 DOCUMENT NUMBER: 131:204460
 TITLE: Steroidal alkaloids and stilbenoids from Veratrum taliense
 AUTHOR(S): Zhou, Chang Xin; Tanaka, Junichi; Cheng, Christopher H. K.; Higa, Tatsuo; Tan, Ren Xiang
 CORPORATE SOURCE: Institute Biotechnology, Department Biological Science Technology, Nanjing Univ., Nanjing, 210093, Peop. Rep. China
 SOURCE: Planta Medica (1999), 65(5), 480-482
 CODEN: PLMEAA; ISSN: 0032-0943
 PUBLISHER: Georg Thieme Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Phytochem. investigation of roots and rhizomes of Veratrum taliense yielded a new and six known steroidal alkaloids as well as a new and one reported stilbene deriv. By a combination of spectral methods (IR, MS, ¹H- and ¹³C-NMR, COSY, HMQC, IMBC, and NOESY), the structure of the new alkaloid was established as 15-angeloylgermane while the known ones were identified as 15-(2-methylbutyryl)germane, jervine, 3-veratrolyzyladenine, germane, veramiline 3-O-beta-D-glucopyranoside and stenophylline B-3-O-beta-D-glucopyranoside. The new stilbenoid, named veraphenol, was detd. to be 2-(3',5'-dihydroxyphenyl)-6-hydroxybenzofuran, and the known one was shown to be resveratrol. The in vitro enzyme assay indicated that 3-veratrolyzyladenine and resveratrol are inhibitors of xanthine oxidase. The enzyme inhibitory action of resveratrol, the most active compd. found so far in V. taliense, is dose-dependent with the IC50 value at 30 μM (the IC50 value of allopurinol used as a pos. control in the study is 10 μM).

IT 469-59-0, Jervine
 RL: BOC (Biological occurrence); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); USES (Uses)
 (steroidal alkaloids and stilbenoids from Veratrum taliense)

RN 469-59-0 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one, 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2002 ACS (Continued)

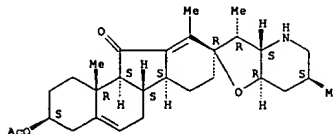
ACCESSION NUMBER: 1999:686451 CAPLUS
 DOCUMENT NUMBER: 123:102413
 TITLE: O-acetylgermane: a new .beta.-adrenoceptor agonist from Veratrum album
 AUTHOR(S): Gilani, Anwar; Aftab, Khalid; Saeed, S. A.; Ali, Rahat A.; Rahman, Atta-ur
 CORPORATE SOURCE: Medical College, Aga Khan Univ., Karachi, 74800, Pak.
 SOURCE: Archives of Pharmacol Research (1995), 18(2), 129-32
 CODEN: APHRDQ; ISSN: 0253-6269
 PUBLISHER: Pharmaceutical Society of Korea
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB I.v. administration of O-acetylgermane (an alkaloid from Veratrum album) produced a dose-dependent (10-100 μg/kg) fall in blood pressure and tachycardia in anesthetized normotensive rats. Pretreatment of animals with propranolol (1 mg/kg) abolished these cardiovascular responses of O-acetylgermane similar to that of isoprenaline (1 μg/kg). In isolated tissue expts., O-acetylgermane (10-100 μM) produced a dose-dependent relaxation of phenylephrine-induced contraction of the rabbit aorta. In guinea-pig spontaneously beating atria, it caused pos. inotropic and chronotropic responses in a dose-dependent fashion (10-100 μM/mL). These responses were abolished in the presence of propranolol (1 μg/mL) similar to that of isoprenaline. These results indicate that O-acetylgermane is a adrenoceptor stimulant (.beta.1 and .beta.2) like isoprenaline.

IT 14788-78-4
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (O-acetylgermane: a new .beta.-adrenoceptor agonist from Veratrum album)

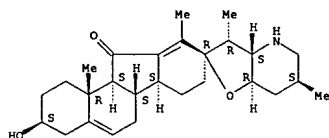
RN 14788-78-4 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(2H)-one, 3-(acetyloxy)-1,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 16 OF 16 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1972:108077 CAPLUS
 DOCUMENT NUMBER: 76:108077
 TITLE: Antiinflammatory activity of jervine
 AUTHOR(S): Gerashchenko, G. I.; Bondarenko, N. V.; Semchenko,
 V. F.
 CORPORATE SOURCE: USSR
 SOURCE: Aktual. Vop. Farm. (1970), Volume Date 1968 169-71
 CODEN: AKVFAM
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 AB Jervine (I) (469-59-0) injected s.c. at 5 mg/kg/day 7 days into rats with
 a paw inflammation, induced by s.c. implanted cotton pellets, decreased
 the granuloma exudate and proliferation by 45 and 41%, resp., and the
 adrenal ascorbic acid [50-81-7] by 30%.
 IT 469-59-0
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (inflammation inhibition by)
 RN 469-59-0 CAPLUS
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one,
 2,3,3'a,4,4'a,5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-
 3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-
 (SCI) (CA INDEX NAME)

Absolute stereochemistry.



=> d ibib ab hitstr 1-9

L5 ANSWER 1 OF 9 USPATFULL

ACCESSION NUMBER: 2002:85565 USPATFULL
 TITLE: Cholesterol and hedgehog signaling
 INVENTOR(S): Beachy, Philip A., Baltimore, MD, UNITED STATES
 Porter, Jeffrey A., Belmont, MA, UNITED STATES
 Cooper, Michael K., Baltimore, MD, UNITED STATES
 PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002045607	A1	20020418
APPLICATION INFO.:	US 2001-954727	A1	20010911 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1999-250785, filed on 12 Feb 1999, PATENTED		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-74714P	19980213 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	LISA A. HAYLE, Ph.D., GRAY CARY WARE & FREIDENRICH LLP, 4365 Executive Drive, Suite 1100, San Diego, CA, 92121-2133	

NUMBER OF CLAIMS: 3
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 7 Drawing Page(s)
 LINE COUNT: 1220

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention sterol-modified hedgehog polypeptides and functional fragments thereof. Methods of identifying compositions which affect hedgehog activity based on inhibition of cholesterol modification of hedgehog protein are described. In one aspect of the invention, the method provides a means for affecting cholesterol biosynthesis or transport in a cell comprising contacting a cell with an effective amount of a compound that affects hedgehog, thereby affecting cholesterol biosynthesis or transport. The effect may be inhibition or stimulation of cholesterol biosynthesis or transport.

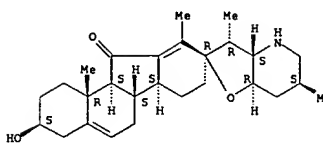
IT 469-59-0, Jervine
 (cholesterol and hedgehog signaling, and modulation of cholesterol biosynthesis and transport)

RN 469-59-0 USPATFULL

CN Spiro[9H-benzo[a]fluorene-9,2' (3'H)-furo[3,2-b]pyridin]-11 (1H)-one, 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 1 OF 9 USPATFULL (Continued)



L5 ANSWER 2 OF 9 USPATFULL

ACCESSION NUMBER: 2002:12550 USPATFULL
 TITLE: INHIBITORS OF HEDGEHOG SIGNALING PATHWAYS, COMPOSITIONS AND USES RELATED THERETO
 INVENTOR(S): BEACHY, PHILIP A., BALTIMORE, MD, UNITED STATES
 COOPER, MICHAEL K., BALTIMORE, MD, UNITED STATES
 PORTER, JEFFREY A., CAMBRIDGE, MA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002006931	A1	20020117
	US 6432970	B2	20020813
APPLICATION INFO.:	US 1998-90622	A1	19980604 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-81186P	19980409 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	ROPER & GRAY, ONE INTERNATIONAL PLACE, BOSTON, MA, 02110-2624	

NUMBER OF CLAIMS: 22
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 7 Drawing Page(s)
 LINE COUNT: 3884

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention makes available assays and reagents inhibiting paracrine and/or autocrine signals produced by a hedgehog protein comprising contacting a cell sensitive to the hedgehog protein with a steroidal alkaloid, or other small molecule, in a sufficient amount to reduce the sensitivity of the cell to the hedgehog protein.

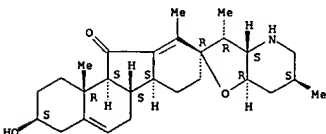
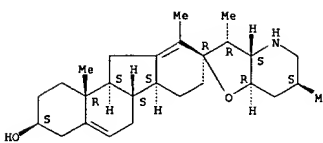
IT 469-59-0, Jervine 4449-51-0, Cyclopamine
 (use of steroidal alkaloid deriva. as inhibitors of hedgehog signaling pathways in relation to effect on cholesterol biosynthesis)

RN 469-59-0 USPATFULL

CN Spiro[9H-benzo[a]fluorene-9,2' (3'H)-furo[3,2-b]pyridin]-11 (1H)-one, 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-octadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 2 OF 9 USPATFULL (Continued)



RN 4449-51-0 USPATFULL

CN Spiro[9H-benzo[a]fluorene-9,2' (3'H)-furo[3,2-b]pyridin]-11 (1H)-one, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-octadecahydro-3'-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 3 OF 9 USPATFULL

ACCESSION NUMBER: 2001:218003 USPATFULL
 TITLE: Stem cells of the islets of langerhans and their use in treating diabetes mellitus
 INVENTOR(S): Habener, Joel E., Newton Center, MA, United States
 Zulewski, Henryk, Geneva, Switzerland
 Abraham, Elizabeth J., Quincy, MA, United States
 Thomas, Melissa K., Boston, MA, United States
 Vallejo, Mario, Madrid, Spain

NUMBER	KIND	DATE
US 2001046489	A1	20011129
US 2000-731261	A1	20001206 (9)

NUMBER	DATE
US 1999-169082P	19991206 (60)
US 2000-215109P	20000628 (60)
US 2000-238880P	20001006 (60)

DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: Kathleen M. Williams, Ph.D, Palmer & Dodge, LLP, One Beacon Street, Boston, MA, 02108

NUMBER OF CLAIMS: 41
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 19 Drawing Page(s)
 LINE COUNT: 2114

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions are described for the treatment of type 1 insulin-dependent diabetes mellitus and other conditions using newly identified stem cells that are capable of differentiation into a variety of pancreatic islet cells, including insulin-producing beta cells, as well as hepatocytes. Nestin has been identified as a molecular marker for pancreatic stem cells, while cytokeratin-19 serves as a marker for a distinct class of islet ductal cells. Methods are described whereby nestin-positive stem cells can be isolated from pancreatic islets and cultured to obtain further stem cells or pseudo-islet like structures. Methods for ex vivo differentiation of the pancreatic stem cells are disclosed. Methods are described whereby pancreatic stem cells can be isolated, expanded, and transplanted into a patient in need thereof, either allogeneically, isogeneically or xenogeneically, to provide replacement for lost or damaged insulin-secreting cells or other cells.

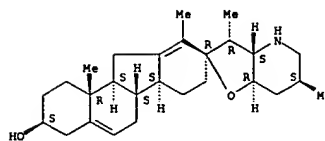
IT 4449-51-8, Cyclopamine
 (isolation, culture, and transplantation of nestin-pos. pancreatic stem cells for diabetes treatment)

RN 4449-51-8 USPATFULL

CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 3 OF 9 USPATFULL (Continued)



L5 ANSWER 4 OF 9 USPATFULL

ACCESSION NUMBER: 2001:188704 USPATFULL
 TITLE: Regulators of the hedgehog pathway, compositions and uses related thereto
 INVENTOR(S): Dudek, Henryk, Wellesley, MA, United States
 Ji, Benxiu, Sharon, MA, United States

NUMBER	KIND	DATE
US 2001034337	A1	20011025
US 2001-867311	A1	20010529 (9)
RELATED APPL. INFO.:	Continuation of Ser. No. US 1999-417564, filed on 14 Oct 1999, PENDING	

NUMBER	DATE
US 1999-115642P	19990113 (60)
US 1999-119594P	19990210 (60)
US 1999-142124P	19990702 (60)

DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: ROPES & GRAY, ONE INTERNATIONAL PLACE, BOSTON, MA, 02110-2624

NUMBER OF CLAIMS: 38
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 19 Drawing Page(s)
 LINE COUNT: 3831

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention makes available methods and reagents for inhibiting aberrant growth states resulting from hedgehog gain-of-function, ptc loss-of-function or smoothened gain-of-function comprising contacting a cell with a compound, such as a polypeptide or small molecule in an amount sufficient to control the aberrant growth state e.g., to agonize a normal ptc pathway or antagonize smoothened or hedgehog activity. The present invention further makes available methods and reagents for ameliorating to consequences of hedgehog loss-of-function, ptc gain-of-function, or smoothened loss-of-function comprising contacting a cell with a compound, such as a polypeptide or small molecule, in an amount sufficient to ameliorate the in certain embodiments, the subject compounds, e.g., a cAMP analog, adenylate cyclase agonist, or cAMP phosphodiesterase inhibitor, regulate cAMP levels, which in turn modulates activity of the hedgehog pathway.

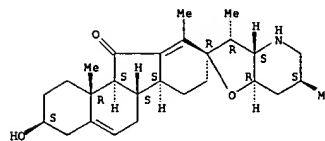
IT 469-59-0, Jervine 4449-51-8, Cyclopamine
 (regulation of the hedgehog pathway and smoothened gain-of-function by gene patched agonists)

RN 469-59-0 USPATFULL

CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one, 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

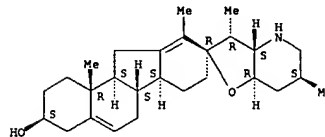
L5 ANSWER 4 OF 9 USPATFULL (Continued)



RN 4449-51-8 USPATFULL

CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 5 OF 9 USPATFULL

ACCESSION NUMBER: 2001:165614 USPATFULL
 TITLE: Stem cells and their use in transplantation
 INVENTOR(S): Moss, Peter Ian, London, Great Britain
 Walters, David Martin, London, Great Britain
 Pointer, Graham, London, Great Britain

NUMBER	KIND	DATE
US 2001024824	A1	20010927
US 2000-731255	A1	20001206 (9)

NUMBER	DATE
US 1999-169082P	19991206 (60)
US 2000-215109P	20000628 (60)
US 2000-238800P	20001006 (60)

DOCUMENT TYPE: Utility
 FILE SEGMENT: APPLICATION
 LEGAL REPRESENTATIVE: Palmer & Dodge, LLP, One Beacon Street, Boston, MA, 02108
 NUMBER OF CLAIMS: 127
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 18 Drawing Page(s)
 LINE COUNT: 2446
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

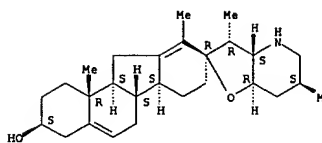
AB Methods and compositions are described for the treatment of type I insulin-dependent diabetes mellitus and other conditions using newly identified stem cells that are capable of differentiation into a variety of pancreatic islet cells, including insulin-producing beta cells, as well as hepatocytes. Nestin has been identified as a molecular marker for pancreatic stem cells, while cytokeratin-19 serves as a marker for a distinct class of islet ductal cells. Methods are described whereby nestin-positive stem cells can be isolated from pancreatic islets and cultured to obtain further stem cells or pseudo-islet like structures. Methods for ex vivo differentiation of the pancreatic stem cells are disclosed. Methods are described whereby pancreatic stem cells can be isolated, expanded, and transplanted into a patient in need thereof, either allogeneically, isogeneically or xenogeneically, to provide replacement for lost or damaged insulin-secreting cells or other cells.

IT 4449-51-8, Cyclopamine
 (isolation, culture, and transplantation of nestin-pos. pancreatic stem cells for diabetes treatment)

RN 4449-51-8 USPATFULL
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

L5 ANSWER 5 OF 9 USPATFULL (Continued)



L5 ANSWER 6 OF 9 USPATFULL

ACCESSION NUMBER: 2001:158338 USPATFULL
 TITLE: Regulators of the hedgehog pathway, compositions and uses related thereto
 INVENTOR(S): Dudek, Henryk, Wellesley, MA, United States
 Ji, Benxiu, Sharon, MA, United States
 PATENT ASSIGNEE(S): Curis, Inc., Cambridge, MA, United States (U.S. corporation)

NUMBER	KIND	DATE
US 6291516	B1	20010918
US 1999-417564		19991014 (9)

NUMBER	DATE
US 1999-115642P	19990113 (60)
US 1999-119594P	19990210 (60)
US 1999-142124P	19990702 (60)

DOCUMENT TYPE: Utility
 FILE SEGMENT: GRANTED
 PRIMARY EXAMINER: Krass, Frederick
 LEGAL REPRESENTATIVE: Vincent, Matthew P., Halstead, David P. Ropes & Gray
 NUMBER OF CLAIMS: 16
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 19 Drawing Figure(s); 19 Drawing Page(s)
 LINE COUNT: 3730
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

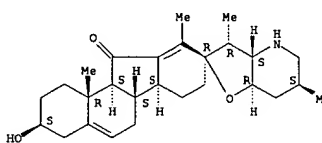
AB The present invention makes available methods and reagents for inhibiting aberrant growth states resulting from hedgehog gain-of-function, ptc loss-of-function or smoothened gain-of-function comprising contacting a cell with a compound, such as a polypeptide or small molecule in an amount sufficient to control the aberrant growth state, e.g., to agonize a normal ptc pathway or antagonize smoothened or hedgehog activity. The present invention further makes available methods and reagents for ameliorating the consequences of hedgehog loss-of-function, ptc gain-of-function, or smoothened loss-of-function comprising contacting a cell with a compound, such as a polypeptide or small molecule, in an amount sufficient to ameliorate the in certain embodiments, the subject compounds, e.g., a cAMP analog, adenylate cyclase agonist, or cAMP phosphodiesterase inhibitor, regulate cAMP levels, which in turn modulates activity of the hedgehog pathway.

IT 469-59-0, Jervine 4449-51-8, Cyclopamine
 (regulation of the hedgehog pathway and smoothened gain-of-function by gene patched agonists)

RN 469-59-0 USPATFULL
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one, 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

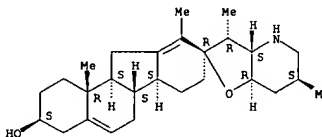
Absolute stereochemistry.

L5 ANSWER 6 OF 9 USPATFULL (Continued)



RN 4449-51-8 USPATFULL
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



LS ANSWER 7 OF 9 USPATFULL

ACCESSION NUMBER: 2001:152946 USPATFULL
 TITLE: Cholesterol and hedgehog signaling
 INVENTOR(S): Beachy, Philip A., Baltimore, MD, United States
 Porter, Jeffrey A., Belmont, MA, United States
 Cooper, Michael K., Baltimore, MD, United States
 PATENT ASSIGNEE(S): The Johns Hopkins University School of Medicine,
 Baltimore, MD, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6288048	B1	20010911
APPLICATION INFO:	US 1999-250785		19990212 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-74714P	19980213 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	GRANTED	
PRIMARY EXAMINER:	Krass, Frederick	
LEGAL REPRESENTATIVE:	Gray Cary Ware & Freidenrich LLP, Haile, Lisa A.	
NUMBER OF CLAIMS:	3	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	11 Drawing Figure(s); 7 Drawing Page(s)	
LINE COUNT:	1222	

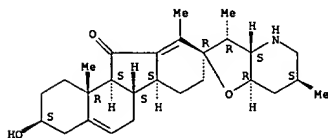
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention sterol-modified hedgehog polypeptides and functional fragments thereof. Methods of identifying compositions which affect hedgehog activity based on inhibition of cholesterol modification of hedgehog protein are described. In one aspect of the invention, the method provides a means for affecting cholesterol biosynthesis or transport in a cell comprising contacting a cell with an effective amount of a compound that affects hedgehog, thereby affecting cholesterol biosynthesis or transport. The effect may be inhibition or stimulation of cholesterol biosynthesis or transport.

IT 469-59-0, Jervine
 (cholesterol and hedgehog signaling, and modulation of cholesterol biosynthesis and transport)

RN 469-59-0 USPATFULL
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one, 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



LS ANSWER 8 OF 9 USPATFULL

ACCESSION NUMBER: 2000:67202 USPATFULL
 TITLE: Method and apparatus for conditioning gas for medical procedures having humidity monitoring and recharge alert
 INVENTOR(S): Ott, Douglas E., 682 Foster Rd., Macon, GA, United States 31210
 Schaefer, John F., Macon, GA, United States
 Gray, Robert I., Macon, GA, United States
 PATENT ASSIGNEE(S): Ott, Douglas E., Macon, GA, United States (U.S. individual)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6068609		20000530
APPLICATION INFO:	US 1998-81186		19980519 (9)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Bockelman, Mark		
ASSISTANT EXAMINER:	Thompson, Michael M		
LEGAL REPRESENTATIVE:	Needle & Rosenberg, P.C.		
NUMBER OF CLAIMS:	42		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	5 Drawing Figure(s); 4 Drawing Page(s)		
LINE COUNT:	991		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An apparatus for conditioning gas for use in a medical procedure, such as endoscopy, the gas being received into the apparatus from a gas source. The apparatus comprises a housing defining a chamber having an entry port and an exit port. A humidification means comprising at least one water-retainer layer is disposed within the chamber in the path of travel of the gas for humidifying the gas as it passes through the chamber. A humidity sensor is disposed within the chamber that senses the humidity of the gas exiting the chamber. A monitoring circuit is connected to the humidity sensor that detects when the chamber requires a recharge of liquid based on the humidity of the gas in the chamber, and generates a recharge signal indicative thereof. A charging port on the housing provides access into the chamber to recharge the chamber with water. A heating element and temperature sensor are also disposed within the chamber. A control circuit further regulates the temperature of the gas exiting the chamber.

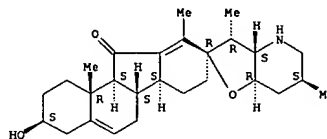
IT 469-59-0, Jervine 4449-51-8, Cyclopamine
 (use of steroidal alkaloid derivs. as inhibitors of hedgehog signaling pathways in relation to effect on cholesterol biosynthesis)

RN 469-59-0 USPATFULL
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one, 2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

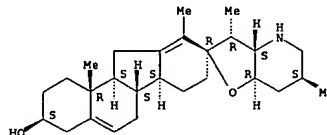
LS ANSWER 7 OF 9 USPATFULL (Continued)

LS ANSWER 8 OF 9 USPATFULL (Continued)



RN 4449-51-8 USPATFULL
 CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3'a,4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 9 OF 9 USPATFULL

ACCESSION NUMBER: 2000:38195 USPATFULL
TITLE: Method and apparatus for rapid determinations of voltage and current in wires and conductors
INVENTOR(S): Singer, Jerome R., 2917 Avalon Ave., Berkeley, CA, United States 94705
Libove, Joel M., 34 Canyon View Dr., Orinda, CA, United States 94563

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6043641		20000328
APPLICATION INFO.:	US 1998-81263		19980519 (9)
RELATED APPL. INFO.:	Continuation-in-part of Ser. No. US 1998-25043, filed on 17 Feb 1998		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Do, Diep N.		
LEGAL REPRESENTATIVE:	Cohen, Howard		
NUMBER OF CLAIMS:	22		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	7 Drawing Figure(s); 3 Drawing Page(s)		
LINE COUNT:	489		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

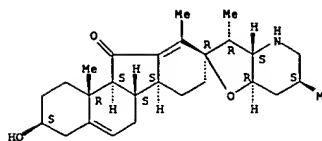
AB A device for non-contact, non-invasive measurement of current or power in a wire, cable or conductor includes a small coil having multiple turns with a thin ferromagnetic strip. The coil may be secured to a wand or housing adapted to be used to place the coil in close proximity to the wire, cable or conductor, whereby a voltage is induced in the coil. An amplifier and/or an analog or digital signal processor is utilized to increase sensitivity. A readout indicates the magnitude of the induced voltage, and a scaling device renders the readout display indicative of the current or power in the wire, cable, or conductor. The readout may comprise a digital display, a series of light emitting devices, an oscilloscope, a digital computer display system, or a flashing light emitting device having a flash rate proportional to the magnitude of the voltage. The device may be constructed in a wand or pen-like fashion, with the coil and strip incorporated into the wand. The device may be combined with a voltage sensor to read out relative voltages.

IT 469-59-0, Jervine 4449-51-8, Cyclopamine
(use of steroidal alkaloid derivs. as inhibitors of hedgehog signaling pathways in relation to effect on cholesterol biosynthesis)

RN 469-59-0 USPATFULL
CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-11(1H)-one, 2,3,3',4,4',5',6,6',6a,6b,7,7',7'a,8,11a,11b-hexadecahydro-3-hydroxy-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

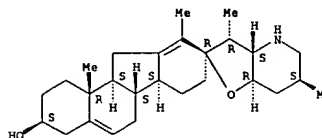
L5 ANSWER 9 OF 9 USPATFULL (Continued)



RN 4449-51-8 USPATFULL

CN Spiro[9H-benzo[a]fluorene-9,2'-(3'H)-furo[3,2-b]pyridin]-3-ol, 1,2,3,3',4,4',5',6,6',6a,6b,7,7',7'a,8,11,11a,11b-octadecahydro-3',6',10,11b-tetramethyl-, (2'R,3S,3'R,3'aS,6'S,6aS,6bS,7'aR,11aS,11bR)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



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(FILE 'HOME' ENTERED AT 06:32:42 ON 11 NOV 2002)

FILE 'REGISTRY' ENTERED AT 06:32:47 ON 11 NOV 2002

L1 STRUCTURE UPLOADED

L2 11 S L1

L3 187 S L1 FULL

FILE 'CAPLUS' ENTERED AT 06:33:50 ON 11 NOV 2002

L4 16 S L3/THU

FILE 'USPATFULL' ENTERED AT 06:36:28 ON 11 NOV 2002

L5 9 S L3